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ELECTRODES FOR FUNCTIONAL ELECTRICAL STIMULATION

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SECTION B. DESIGN AND FABRICATION OF ELECTRODES, LEADS AND CONNECTORS

B.2.4.1: Silicone Rubber Sheeting

The goal of this project was to establish performance specifications for the silicone rubber sheeting used in the spiral cuff electrode fabrication. Tests were conducted to determine the mechanical and physical properties of four different silicone rubber sheeting formulations. Additionally, we investigated the effects of aging and sterilization on these properties.

Results from testing were reported in periods 6, 7 and 8. Data from those periods were analyzed further to establish the working parameters of the silicone rubber sheeting for the cuff electrode application. The maximum strains that the materials undergo during fabrication are illustrated on Figure B.1 on the following page. It can be seen from the graph that the maximum strain used in cuff manufacture is within the elastic range of the materials. Specifically, the MED-4550 is subjected to a strain of 1.138, MED-6640 is subjected to a strain of 1.629, and MED2-6641-1 is subjected to a strain of 2.245. Any of these materials could be used for this application without incurring failure of the silicone.

We initiated a project during this period to determine experimentally the relationship between strain and final cuff diameter for three different types of cuffs. The components of these cuffs are shown in the chart below. All of the cuffs will be made using MED-4550 sheeting.

1	2	3
stretched 50 μm	stretched 75 μm	stretched 50 μm
unstretched 50 μm	unstretched 50 μm	unstretched 50 μm
elastomer 50 μm	elastomer 50 μm	
unstretched 50 μm	unstretched 50 μm	
unstretched 50 μm	unstretched 50 μm	

These cuffs are to be manufactured at four different strains. These strains were chosen to be at 25, 50, 75, and 100 percent of the calculated strain using Naples equation. The diameters of the resulting cuffs will be measured. The averages of the data will be plotted showing standard deviations. This plot can then be used to fit a regression line, which will approximate the strain necessary to make a cuff of a desired diameter. The third cuff type has been manufactured and measured as seen in Figure B.2.

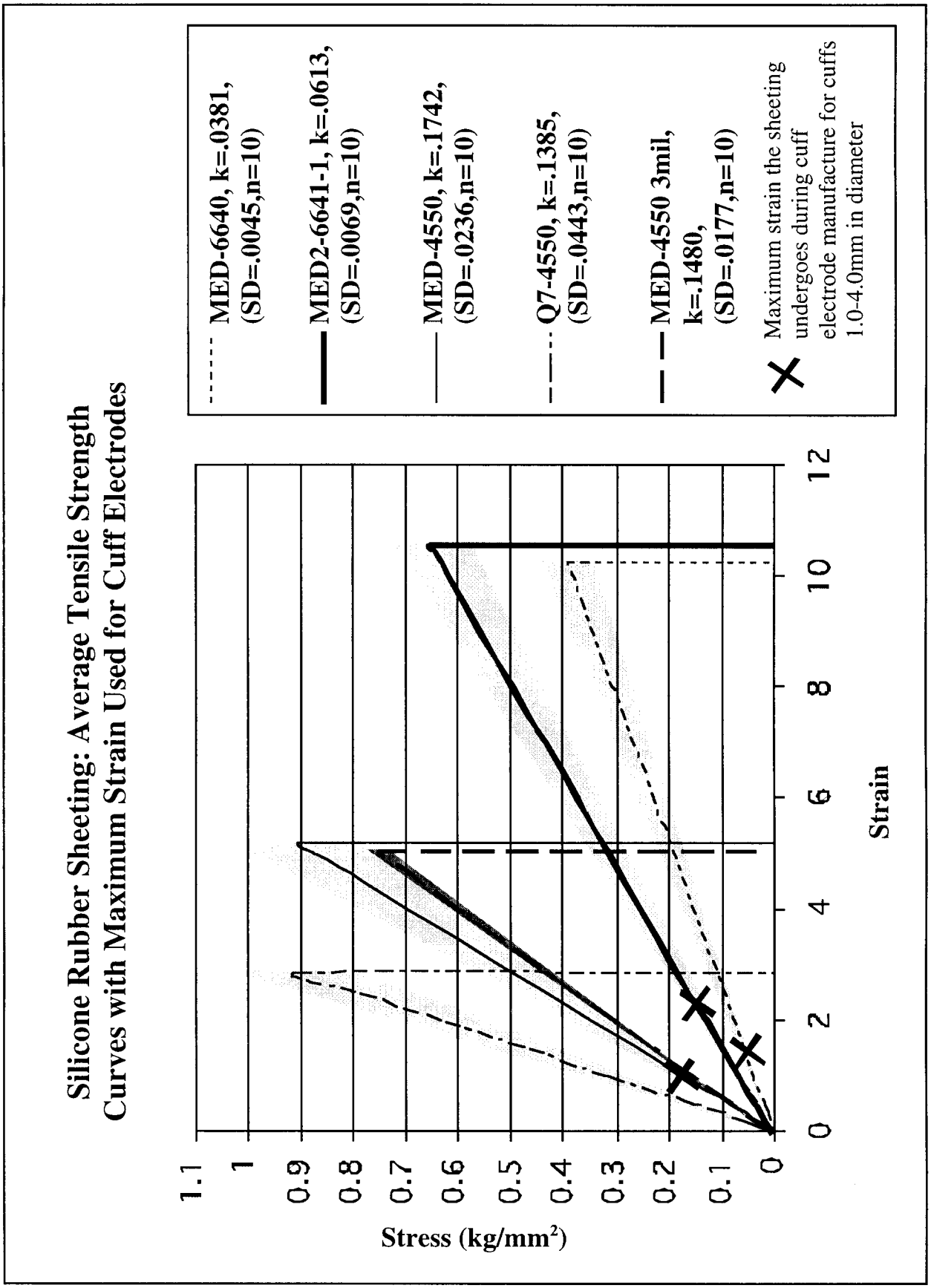

Figure B.1: The graph above shows the tensile strength curves for the four different silicone rubber sheeting formulations tested. In addition, the maximum strain that the sheeting undergoes during PMP cuff electrode manufacture is represented by the X's.

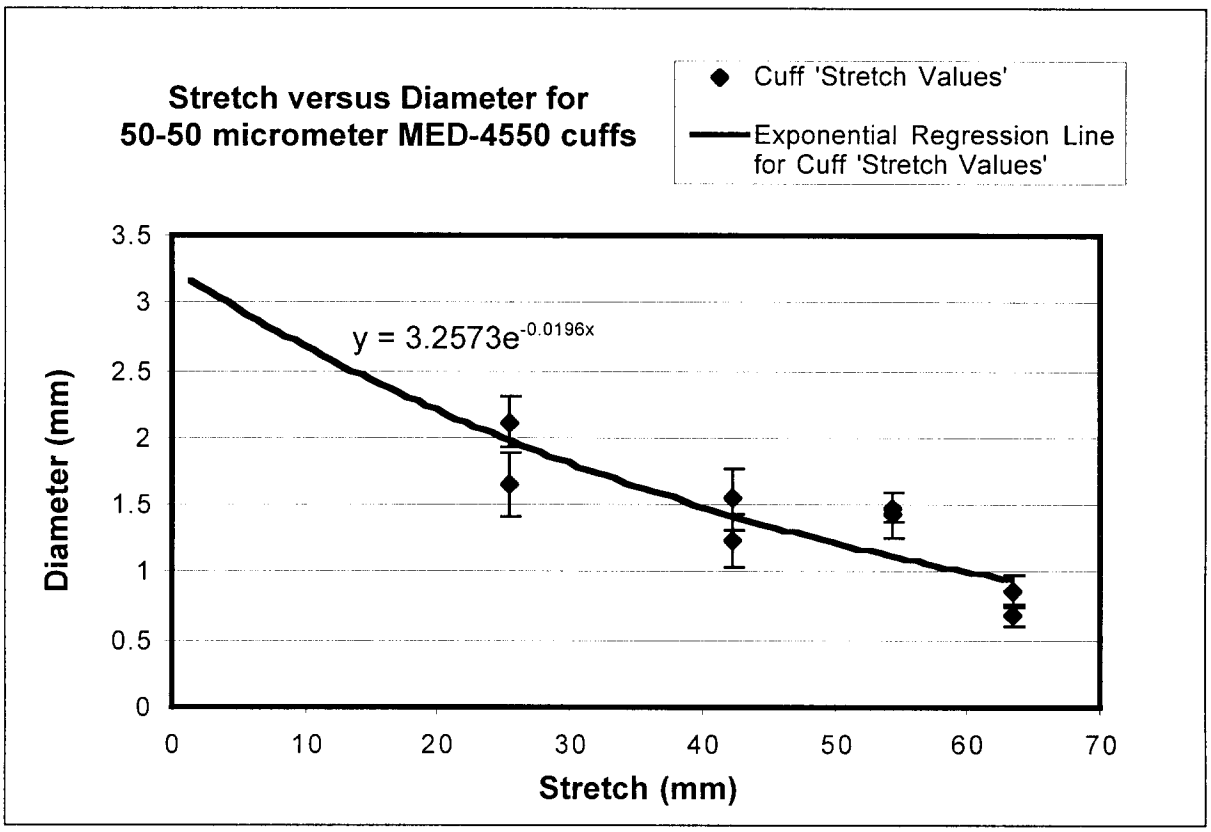

Figure B.2: Two laminations were made at four different stretches. Cuffs were cut from these laminations and their diameters were measured. The averages of the cuffs for each lamination are represented by the diamonds on the graph. The cuffs were made of two 50 μm thick sheets of MED-4550 silicone. The regression line can be used to determine the approximate stretch needed to obtain a particular diameter for this cuff configuration. Note: "stretch" is the difference between the original length of the silicone sheet and its final length (126.8 mm).

Another silicone rubber sheeting test that was implemented in this period was a simulated aging test to determine the change in cuff diameter over time. This test was developed to determine if silicone rubber cuffs undergo relaxation with *in vivo* aging. In order to attempt to simulate this, cuffs were soaked in a bath of phosphate buffered saline solution at 85°C for 28 days. A gas mixture representative of that in vivo (2% O, 5% CO_2, 93% N) was continuously bubbled through the bath. The diameters of the cuffs were measured at five intervals over the course of this test and were measured both wet and dry.

Samples Silicone rubber cuffs were made of the layers described below:

75 μm MED-4550 stretched
50 μm MED-4550 unstretched
50 μm MED-4210 elastomer
50 μm MED-4550 unstretched
50 μm MED-4550 unstretched

Note: the stretch lamination was performed using MED2-4013 adhesive.

Eight samples from five different 3.0mm cuff laminations were made by cutting cuffs that have eight different widths and that are between 1/2 and 1 full wrap. The eight cuffs were labeled by different "tail" lengths. The cutting procedure for the cuffs and "tails" is described below.

Procedure for Silicone Cuff Cutting

1. Eight cuffs were cut per lamination. The range of cuff heights, used for labeling purposes, were 4.0 mm to 11.0mm with increments of 1.0mm. The extra height above 4.0mm for each cuff was cut into a "tail". This tail consisted of two slits that separated the tail from the 4.0mm portion, which was used to obtain the diameter measurements. Each slit was cut perpendicular to the side of the cuff and approximately a third of the way over across the length of the cuff, leaving a third of the original length in between the slits. The position of the slits in terms of height is equivalent to the width of the smallest cuff. Schematics of the eight cuffs and their respective "tails" are shown below this section.
2. The cuffs were cut to yield approximately 90% of the first full wrap of the cuff to enable diameter measurements to be made without frictional or compressive forces from overlapping layers. For this particular set of cuffs, this length was between 6.5 and 7.5mm.
3. Using a metric ruler (w/mm divisions), individuals cuffs were cut to the specified widths and approximate range lengths to the nearest mm. Note: Lengths were measured to the nearest mm using a ruler but were estimated to the nearest 0.1 mm by eye.
4. After an individual cuff was cut, its inner diameter and top space were measured to the nearest 0.1 mm using a gradicule.
5. Note: Inaccuracy in measurement is possible due to any uneveness along the border of a cuff resting on the gradicule. In addition, the silicone's flexibility and inclination to slightly stick to any surface it is in contact with may cause the cuff's measurement to be somewhat contracted or expanded while on the gradicule.

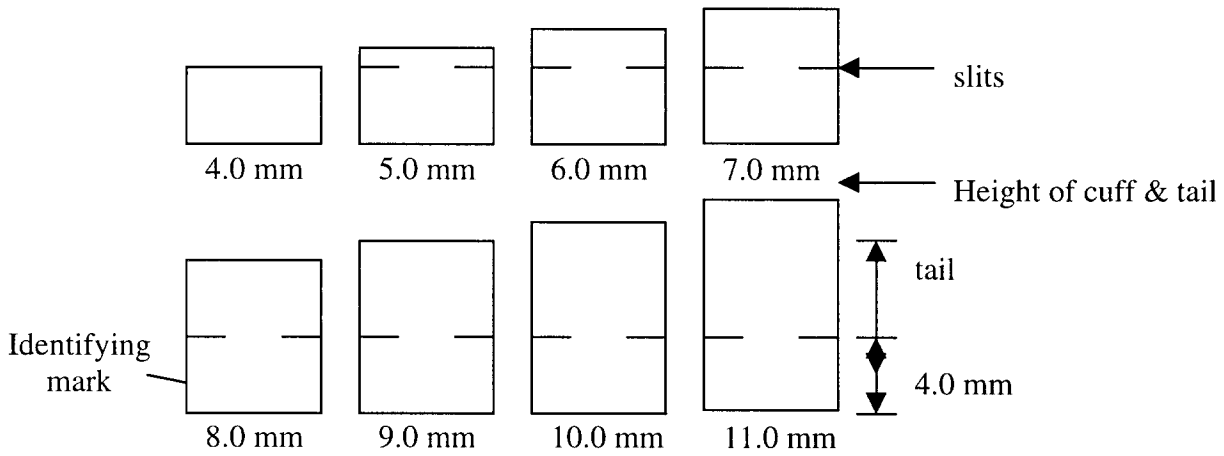

Figure B.3: Representation of label system for cutting the silicone rubber cuffs.

Set-up & Procedure

The cuffs were placed in five different flasks (eight samples from one cuff lamination per flask). The flasks contained phosphate buffered saline solution and were sealed with a rubber stopper. The rubber stoppers had inlet and outlet ports for gas flow to be bubbled through continuously. The gas mixture used was 2% O and 5% CO_2 in N. The five flasks were placed in a water bath held at 85°C.

The diameters of each cuff were measured and recorded using a microscope and a gradicule at 0,7,14,21,and 28 days. The diameters were measured "wet" and "dry". The cuffs were considered "wet" when they had absorbed 0.4% of their initial mass, per data obtained from Avecor, Inc. This mass was reached after being soaked in Ultrapure water at room temp for 15 minutes. The cuffs were considered "dry" after sitting in a dessicator with a vacuum for 15 minutes (i.e. the extra 0.4% mass of water was removed). The diameter measurements were taken according to the drawing below. The cuffs remained in the temperature bath at 85°C for 28 days.

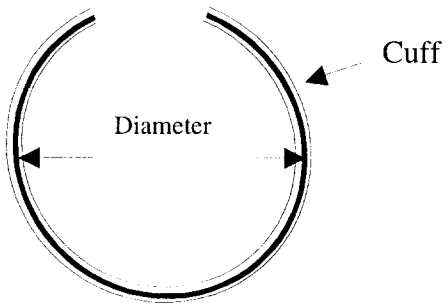

Figure B.4: Schematic of cross section of cuff showing proper diameter measurement.

Results

The data were analyzed for wet and dry measurements over the 28-day period. The chart below contains the average diameters and their standard deviations for all of the cuffs tested at the five measurement intervals.

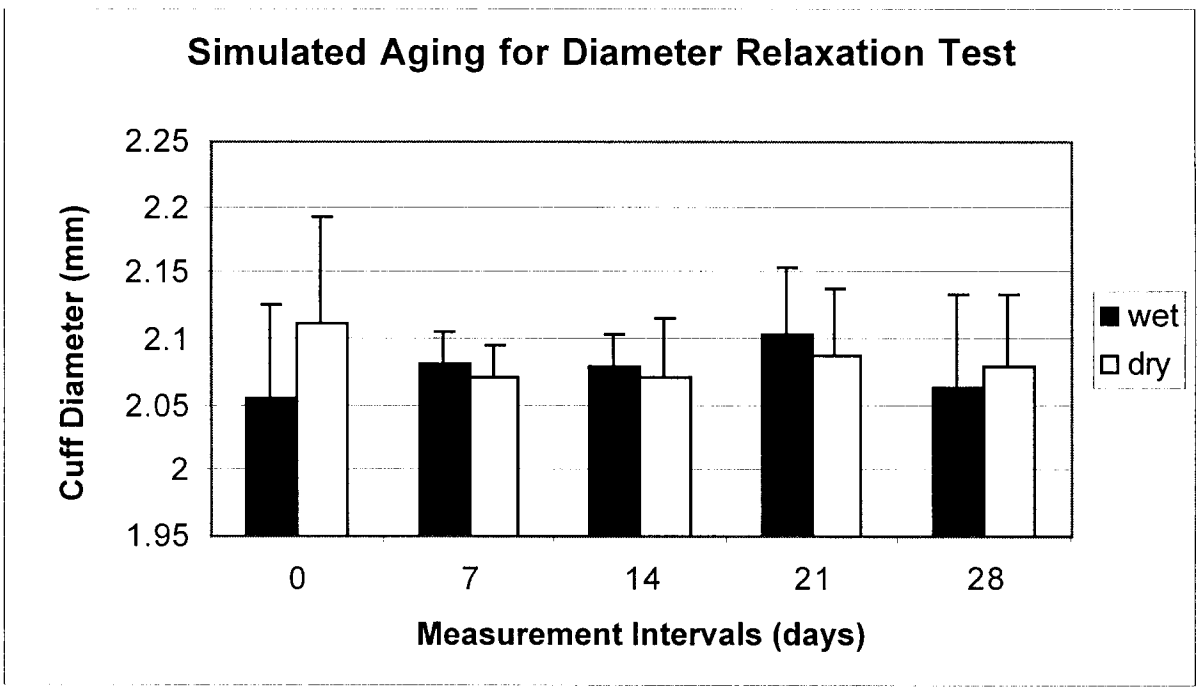

Figure B.5: Averages and standard deviations for the diameters of the silicone rubber cuffs over the 28-day simulated aging period.

It was found that there was no statistically significant change in the diameters of the cuffs over the 28-day period. There is also no statistical difference between measuring the cuffs wet and measuring them dry.

Future Work

The strain versus diameter relationship will be explored further by completing types 1 and 2 of the cuff manufacture. These data will be discussed in period 10. Specifications for the formulation, or combination of formulations that should be used in cuff manufacture will be given upon testing completion.

B.2.5.1 Flexion Testing

Rolling Test

This test was developed in order to determine whether the electrode would incur breaks and/or lose its conductivity after being opened 100 times. It was estimated that an average electrode would be opened completely, and held flat, no more than 10 times during manufacture, cleaning, and implant. Performing this test 100 times allows for a safety factor of 10. Five electrodes were tested.

Set-up and Procedure

1. The cuff electrode's inner diameter was measured as 3.0mm. In order for a rod to be glued, with MED-1137 silicone adhesive, to the electrode without interfering with the platinum electrode, it was determined that the rod should be glued to the silicone rubber end of the cuff, thereby placing the platinum in the outer wrap. In order to maintain a diameter of 3.0mm, it was calculated that the rod used would need to be 2.725mm in diameter.
2. A metal rod with approximately same diameter was found and glued to the silicone end of the cuff parallel to the edge. The rod and cuff were left overnight to let the glue dry.
3. The following day, the resistance, between the stimulation site and it's lead wire was measured for each of 4 contact sites. The lead wires for the five electrodes were approximately 31 cm in length and yielded an average 6.77 ohms per cm of resistance.
4. The end of the electrode away from rod was held down manually, and the rod was rolled across the electrode so that the electrode cuff would wrap around the rod. The rod was then rolled back to unwrap the electrode from around the rod and lie flat. This constituted one cycle.
5. After 10 cycles, the resistance of each of the 4 contact sites for electrodes were measured and recorded.
6. 10 sets of 10 cycles were performed for a total of 100 cycles.
7. This process was repeated for four additional electrodes.

Results

The rolling test was performed on five electrodes. The resistances were measured for each stimulation site on the five electrodes. The averages and standard deviations for the five electrodes at each of the four stimulation sites are shown over the 100 cycles in the chart below.

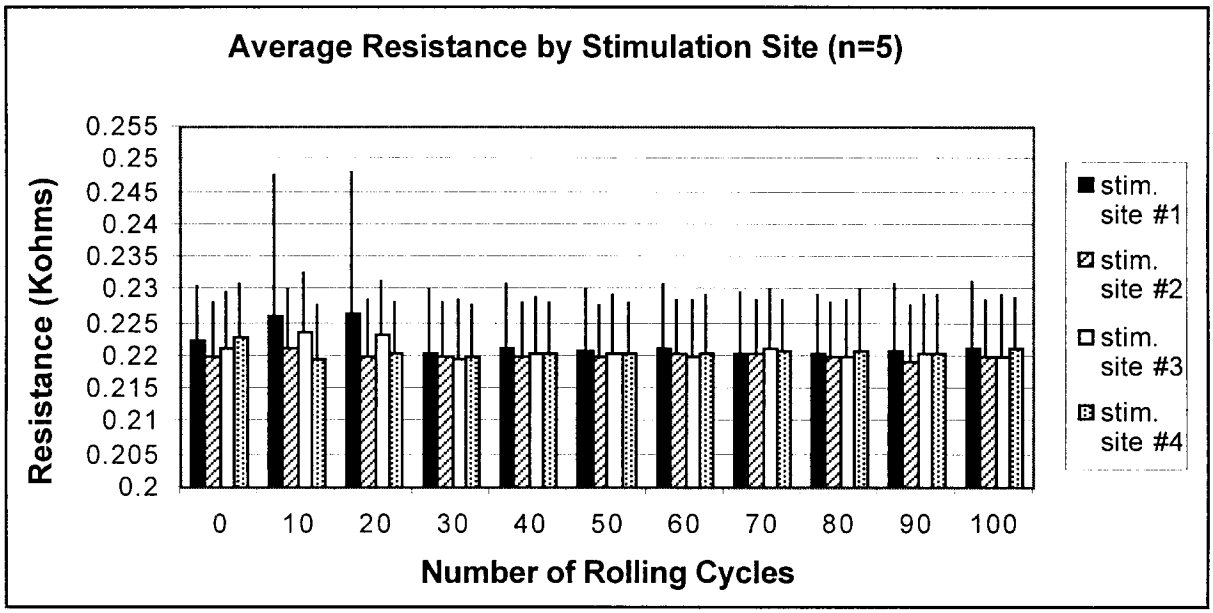

Figure B.6: Resistance measurements for each of the four stimulation sites over the 100 cycles tested. The measurements from five electrodes were averaged.

The data shown in this chart are interpreted to indicate that there was no significant increase in the resistances of the electrodes over the 100 cycles. An increase in resistance would have indicated a crack or break in the platinum conduction paths. All of the electrodes were examined using microscopy after the testing was complete. No breaks were detected in the platinum of any of the electrodes. Scanning electron microscopy was performed on the stimulation sites of three of the electrodes to determine if any damage was caused by taking the resistance measurement. The microscopy revealed no damage on the stimulation sites other than scrapes occurring from site removal.

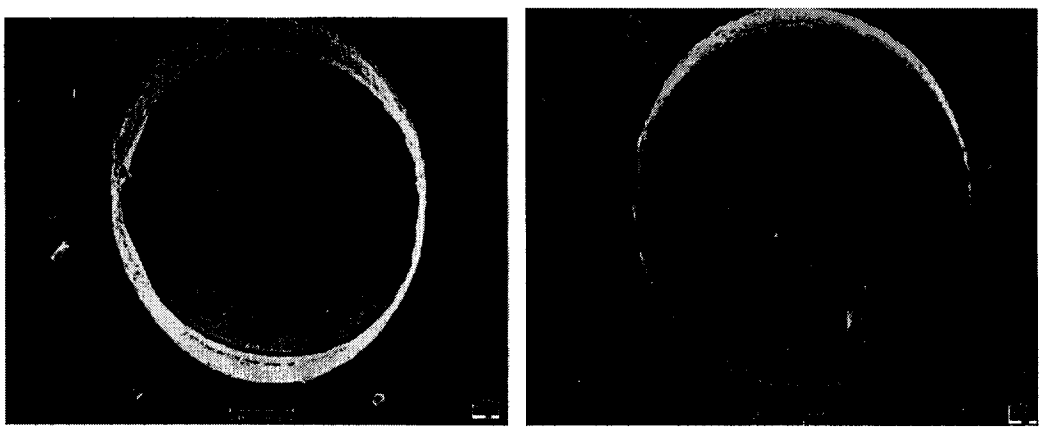

Figure B.7: The two pictures above are of PMP3 electrode stimulation sites using scanning electron microscopy. The few scrapes seen in the picture on the right are believed to have been caused by forceps scraping the platinum during removal of the silicone rubber. The method used to measure the resistance, touching a wire to the stimulation site, did not change the appearance of the platinum.

Simulated Aging with Flexion Test

In order to determine the effect of mechanical movement while aging on silicone rubber cuffs, the following test was developed. Five sets of 8-10 cuffs will be placed five flasks containing a phosphate buffered saline solution held at 85°C for 28 days. Each cuff will be 4 mm in width and at least 10 mm in length. A gas mixture of 2% O, 5% CO_2, and 93% N will be continuously bubbled through the flasks. The flasks will be set on a hot plate/stirrer. A magnetic stirrer bar will be placed in each flask and will stir the solution causing the cuffs to undergo mechanical movement. After the 28-day period, the cuffs will be removed and tensile tested to failure. The gage length of the cuffs will be 8 mm. Control cuffs which have not been aged will also be tensile tested.

In addition to testing the cuffs, samples of 75 μm thick silicone sheeting will undergo the same test as above. Sample groups of the sheeting will be control (no aging), aged, and aged with stress. The aged with stress group will contain pieces of silicone rubber sheeting that have been stretched and placed in a frame during aging. Dots of adhesive will be placed on the sheeting before stretching in order to illustrate the change in length after the stretch and after aging. Sample size for this test will be determined using the variability from previous 75 μm tensile tests.

Future Work

The simulated aging test with flexion began in this period for four electrodes and cuffs. Results from the 28-day test will be reported in period 10. The aging test for the stretched and unstretched sheeting will be performed and reported in period 10.

B.2.5.2 Corrosion Testing

Samples

Two sets of four electrodes will be tested for corrosion. One set will contain electrodes that have undergone simulated aging. These will be the four electrodes tested in the Simulated Aging/ Flexion test of Section B.2.5.1. The other set will contain two electrodes that were used in the rolling test (Section B.2.5.1). These samples represent electrodes that have been flexed beyond what is expected during manufacture and implant. They will provide information on the relationship between fatigue from flexion and corrosion. The remaining two samples will be unused. Meaning they have not been flexed, aged, or tested since manufacture.

Stimulation

Four electrodes (sets of two running in parallel) will be pulsed at the maximum expected stimulus parameters. Specifically, they will be pulsed continuously at 30 Hz with biphasic constant current rectangular waveform at 5 mA with 10μs pulsewidth and 0 interphase delay. One electrode (4 contacts) will receive 3 anodic currents and 1 random control (no pulsing). The second electrode will receive 3 cathodic currents and 1 random control. The resulting voltage between each electrode contact and a saturated calomel reference electrode will be measured using high input impedance (10^{12} Ω) buffer amplitudes and an RMs voltmeter. These measurements will be taken twice each week. The electrode impedance will then be plotted as a function of time over the 28-day test period.

Bath & Medium

The test will be run in a bath of phosphate buffered saline solution. A gas mixture of 2% Oxygen, 5% Carbon Dioxide, and 93% Nitrogen will be continuously bubbled through the flasks. Ultrapure water will be added to the flasks as needed.

Testing

The amount of platinum in solution will be tested before the test begins and after the 28 day period. SEM will be performed on a control group of three electrodes (12 stimulation sites) that have not been tested. Microscope inspection and SEM will also be performed on the stimulation sites of the tested electrodes (32 sites) and on any suspected corrosion sites (remove insulation). This evaluation will take place after the 28-day test period. Deposits of corrosion will also be examined for elemental composition using EDAX. The electrodes will also be examined for delamination.

Future Work

The two sets of corrosion tests will be performed and reported in period 10.

B.2.6 *In Vivo* Testing

The *in vivo* testing to be performed in this contract consists of three PMP electrodes implanted in cats for 3 months each. Three PMP3 electrodes are currently *in vivo* and will be explanted for analysis upon completion of stimulation testing performed according to Section C.I.2.2 of this report. As reported in period 8, one PMP2 electrode that had been previously implanted was found to have a break in the platinum. This break was evaluated using scanning electron microscopy in order to characterize the mode of failure.

Figure B.8: The top picture shows the break in the platinum path. The silicone was removed from the platinum surrounding the break. The dark surrounding material is the silicone rubber. The bottom two pictures focus on the break itself. The picture on the left reveals a dent in the middle of the top end and a scrape in the bottom. These could have been caused by the scalpel blade during silicone removal. The bottom right picture shows that there is a bevel in the platinum. What caused the bevel is unknown, but that is the likely cause of the break itself.

The break above has the same characteristics as the break analyzed from the PMP2 electrode that was not implanted. Due to the bevel in the platinum at the point of the break, it is believed that the break may have occurred due to an application of pressure at that point. This may have weakened the material and caused it to break. As explained in period 8, this break was probably induced during the final cleaning procedure, handling, or implant. The PMP3 design has proven to be more robust in handling, and has yet to incur any such breaks or problems.

Future Work

Upon stimulation completion, the electrodes will be explanted and tested according to the contract proposal.

SECTION C. IN VIVO EVALUATION OF ELECTRODES

C.I.2.2: Selective Activation Stability Over Range and Time; Chronic Animal Tests

Abstract

The objective of this project is to qualify nerve cuff electrodes for use in human subjects. We have two designs that we believe are or will be technologically feasible and reliable, the PMP design and the wiggle-wire design. The first design, the PMP electrode, contains a sheet of platinum that is cut with a laser and embedded into the silicone rubber to produce a thin, multi-contact nerve cuff electrode. The wiggle-wire electrode is produced with the lead wires being bent back and forth in the plane of the electrode to allow the conductor to accommodate compression and tension during flexion of the cuff.

Chronic experiments, designed to provide both histological data on the safety of these electrode designs and stimulation results on the long-term stability of the recruitment properties of the electrodes, were begun. The stability of stimulation from a single position (i.e. an individual tripole) was previously tested by Grill [1996]. The stability of more complicated electrode configurations involving contacts at multiple locations were not tested. During the course of these experiments, we are testing field steering techniques to verify that their properties stabilize over time.

Progress

A total of nine implant procedures have been performed. A summary of the nine implants is illustrated in Table C.1. As shown in Table C.1, one animal did not survive the surgery. Three additional animals were terminated early. One animal due to a serious skin condition and the other two animals due to suspected electrode complications. Two possible explanations for the electrode complications include the electrode became dislodged from the nerve partially or fully, or electrode leads or conductivity paths may have broken. Upon explant, both electrodes were still located on the nerve with no noticeable abnormalities. Post-explant examination did find one of the electrodes (Cat #552) to have a break in a conductivity path (see section B.2.6), no such break, however, was located in the second electrode (Cat #535).

Analysis of the data from both the five remaining animals and the animal terminated at seven weeks (Cat #380) has been started. Qualitative analysis, similar to the graphs presented in PR#7, suggest that repeatable results are possible between weeks. Quantitative analysis based on techniques used by Grill *et al.* 1998 will be implemented. Additional analysis to expand the analysis is also being investigated. These results should be prepared during the next reporting period.

Table C.1: A summary of the nine chronic implants. For each implant procedure a summary of the date, electrode implanted, and current status is provided. In one case (*) no electrode was implanted due to the loss of the animal during the procedure (as noted in the table). The electrode abbreviations refer to the wiggle wire (WW) electrode and the Platinum-Metal-Platinum electrodes versions 2 and 3 (PMP2 and PMP3). The reported number of weeks for electrodes implanted is up to and including 4/1/99.

Cat #	Implant Date	Electrode Type	# of Tests	Explant Date (# of wks)	Comments
380	5/20/98	WW	3	7/8/98 (7)	Skin condition mandated early termination
399	6/24/98	WW	9	(40)	
545	7/29/98	*	0	7/29/98 (0)	Animal died during surgery
535	9/1/98	PMP2	2	10/14/98 (6)	Stimulation complications
552	9/15/98	PMP2	2	10/15/98 (4)	Stimulation complications Breakage found
553	11/10/98	WW	5	(20)	
555	12/3/98	PMP3	5	(17)	
576	12/8/98	PMP3	4	(16)	
569	12/16/98	PMP3	4	(15)	

C.I.2.3: Continuous Torque Space

Abstract

The objective of this project is to develop methodologies, suitable for use with cuff electrodes, to effect contraction of multiple muscles, at different levels of activation, to produce a range of torque output in the physiological torque space. Activation of multiple muscles can be achieved using stimulation from multiple contact. The region of stimulation can be steered between different fascicles by varying the level of stimulation at each contact. Previous work indicates that the multiple fields interact resulting in a final area of excitation that is different than the logical summation of the two individual stimulation. Multiple muscle activation can also be achieved by using two different contacts stimulated with a short delay between the pulses to avoid field effects from the combination of pulses. The delay must be long enough to allow partially depolarized axons to return to their resting state but short enough to stay within the refractory period of the axons that were fully depolarized. Work performed during this contract suggests a delay of 900μs as the standard can be used to produce two independent stimulation pulses. Presently, the resulting output from two stimulations with a 900μs delay is being compared to a linear summation of each individual pulse.

Progress

A foreseeable usage for nerve cuff electrodes is for the user (patient, engineer or doctor) to desire a particular torque output. The desired torque output should be produced with minimal co-contraction. The problem is under-constrained and therefore multiple solutions exist. One method is to test all possible combinations and use a look-up table or a neural network to achieve the desired output. Another approach is using stimulation from different contacts that produce activation of different nerve fibers to be used together to produce a range of torque outputs.

Simultaneous stimulation from multiple contacts has been found to produce a range of torque output. In work previously reported from this contract, PR# 5, we found that varying the amplitude of the stimulation from multiple contacts can produce a range of torque outputs that were representative of stimulation of multiple fascicles. A smooth and continuous transition of torque output was apparently achieved. The output torque produced by the simultaneous stimulation from multiple contacts, however, was not found to be a linear summation of the torque outputs from each individual stimulation. Figure C.1 illustrates the non-linearity of this simultaneous stimulation. In Figure C.1, the torque output from contact 0° was found to produce a torque output similar to the tibial (Tib) nerve branch. The torque output from contact 270° was found to produce a torque output similar to the lateral gastrocnemius (LG) nerve branch. The simultaneous stimulation from both contacts was found to produce more lateral rotation than either the 0° contact or the 270° contact produced individually or linearly added together. The small cluster of points near the origin is the predicted output of the summed torque output from the two contacts at each of the current amplitudes that were used during the simultaneous stimulation. The amplitude of the summed output also did not come close to the output torque achieved using simultaneous stimulation. In the upper left corner of Figure C.1 is a diagram illustrating the non-linear summation of stimulation. The white area around each electrode represents the areas that are stimulated by each contact when stimulated individually. The shaded area represents an area that was partially depolarized but does not reach a level to create a propagating action potential. When both locations are stimulated simultaneously, the region of overlap is partially excited by both regions to a level that may now create a propagating action potential. These results agree with both modeling work and experimental work that has been performed in both this laboratory and other laboratories.

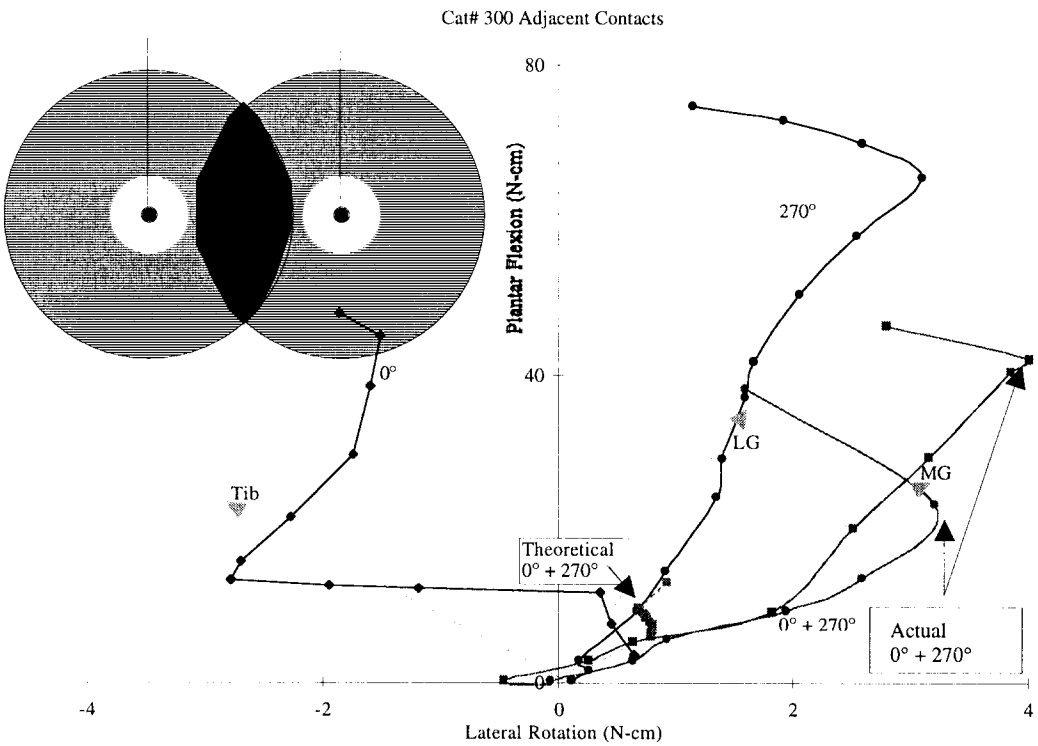

Figure C.1: An illustration of how simultaneous stimulation does not result in a linear summation of torque outputs. Individual stimulation from both the 0° and the 270° positions are shown to produce similar torque output as the Tib and the LG branches respectively. The simultaneous stimulation from both the 0° and the 270° positions is shown to produce more Lateral Rotation than either position alone. The theoretical summation of the individual torque outputs for each amplitude used during the simultaneous stimulations are represented by the cluster of points near the origin. The upper left illustrates how two electrodes that individually activate the areas in white and partially depolarize the shaded regions can activate a larger area when stimulated together.

The second approach is based on previous work [Peckham 1972, Rutten *et al.* 1991, Yoshida and Horch 1993] that found the refractory period of an axon (time after an action potential during which the axon can not produce another action potential) is longer than the facilitative period (time during which an axon remains partially depolarized when the stimulation does not create an action potential). Using a delay that is greater than the facilitative period but within the refractory period, we hope that two stimulation pulses could be used to produce an additive output. Since previous work was performed in different species [Peckham 1972] or using different electrode types [Peckham 1972, Rutten *et al.* 1991, Yoshida and Horch 1993], experiments using a nerve cuff electrode in the cat were performed. Preliminary work indicates that a delay of 900μs fell outside the facilitative period but within the refractory period. During this period additional data was taken to determine if this window is sensitive over time or location around the nerve trunk. Preliminary results from these data indicate that 900μs delay is within the widow for all locations, amplitudes and times.